

## NON-TECHNICAL ABSTRACT

In the United States, it was estimated that 132,000 new cases of colorectal cancer would be diagnosed in 1998, and approximately 40% of those patients will eventually die from the disease. Colorectal cancer most commonly spreads to the liver. The p53 gene is frequently altered (either abnormal or absent), in the tumors of patients with colorectal cancer. The incidence of p53 gene mutation has been reported in at least 75% of colorectal cancers. In experiments using cells in test tubes and in animal models, introduction of a normal copy of the p53 gene into cancer cells that have an abnormal p53 gene has been shown to decrease tumor growth.

The current standard treatment for colorectal cancer with metastases to the liver includes systemic chemotherapy (administered through a vein so that it can circulate throughout the entire body) and intrahepatic chemotherapy (administered through an artery that goes directly to the liver). Patients with colorectal cancer that has spread to the liver and is not able to be surgically treated will live for approximately 6-12 months.

SCH 58500 is a novel form of treatment called "gene therapy". SCH 58500 uses a virus to deliver the normal gene into a tumor that has lost normal gene function. The modified virus has been constructed from an adenovirus most frequently associated with the common cold. The virus has been modified so that the parts of the virus necessary to reproduce itself have been removed and replaced by the normal p53 gene. The virus is not expected to be able to multiply in the patient.

This study is designed to evaluate any additional efficacy of SCH 58500 to standard chemotherapy in patients with colorectal cancer that has spread to the liver and whose tumors have an abnormal p53 gene. All patients in this trial will receive standard chemotherapy. Half of the patients in this study will receive SCH 58500 in addition to chemotherapy. This trial will also continue to evaluate the safety of SCH 58500 when combined with chemotherapy.